

AN ATYPICAL CASE OF MULTIPLE SCLEROSIS.*

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Mr. D. was examined by us at the Home for Incurables, in September, 1899. We saw him once only. He stated that he was forty-six years old, single, and with no vicious habits. He denied having used alcohol even moderately. His health previous to his present illness had always been good and he had never had any venereal disease. The onset of his present trouble was slow; its course progressive and steadily downward. Seven years ago he began to have difficulty in walking, and now cannot move his legs at all. He has not been able to walk or even stand for several months. He has never had any pain in the legs. He has, at times, had slight spasmodic retention of urine, but has never been catheterized. During the past year his bowels have been moved only after the use of purgatives.

Examination.—He is a man of excellent build, chair-ridden, and unable to move either leg, as much apparently on account of spasm as because of palsy. The spasm in the legs is greatly increased by attempts at passive movement. The knee-jerks are very much exaggerated, ankle clonus is present, and the plantar and cremasteric reflexes are very marked. A tap anywhere on either leg causes a clonus to appear in the whole extremity. Motion in the arms is good (later he complained that the arms had become a little weak) and the grip is strong. There is no ataxia nor rigidity in the arms. Sensation is normal over the entire body. There are no cranial nerve palsies. The heart and lungs are normal. There is no wasting of the legs, indeed the legs are, if anything, more developed than the arms. The left great toe is in constant extension and the left foot is inverted on the ankle. There are no trophic changes of the skin, joints, or nails. There is no difficulty in speech or mental defect. Gastric or other crises, headache, girdle sense, vertigo and vomiting are all absent.

Dr. Charles K. Mills at one time treated the patient, and has kindly sent us the following notes: "The first notes were

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made June 12, 1895. For three years previous to coming under observation he had been annoyed at times by numbness both in his left and right hands, but more marked in the former, and he had had increasing difficulty in doing such acts as buttoning his collar, especially with his left hand. He had also gradually lost the power of properly controlling the movements of his lower limbs, especially of his right leg, which, as he then expressed it, showed a tendency to flop around. He found it necessary to see the ground in order to walk without staggering. He could not balance himself well, even with his eyes open. He was weak in the legs and, as compared with his condition of a year or two previous, he was neurasthenic and easily exhausted. He complained that he could not hold his urine as well as he had done, and of some haziness of vision; he had no diplopia, however. No history of lancinating or other pains could be elicited, and he had no sensory symptoms except the numbness above described. Touch, pain and temperature sensations were preserved. Knee-jerks were exaggerated, and ankle-clonus was probably present, although I did not discover this until a subsequent visit. Briefly, the symptoms presented by the patient at the time of my first examination were: Moderate ataxia in both the lower and upper extremities, a general neurasthenic state, exaggerated, deep reflexes and absence of all sensory symptoms except some numbness in the hands, especially in the left. I saw the patient at intervals in 1896 and 1897, and again a few months before his death, in 1899. In March, 1896, I examined him, in consultation with Dr. S. Weir Mitchell. At that time he had the symptoms above described, with marked ankle-clonus. He grew more and more ataxic and paretic, and finally was compelled to give up active employment, probably in the latter part of 1897, although I am not sure as to the time. It is interesting to note that although he was markedly ataxic and paretic during 1896 and 1897, spasticity was not present, or at least was not of a decided character. When I saw him a few months before his death he was helpless, emaciated, with marked spasticity and contraction of his limbs, although in full possession of his intelligence."

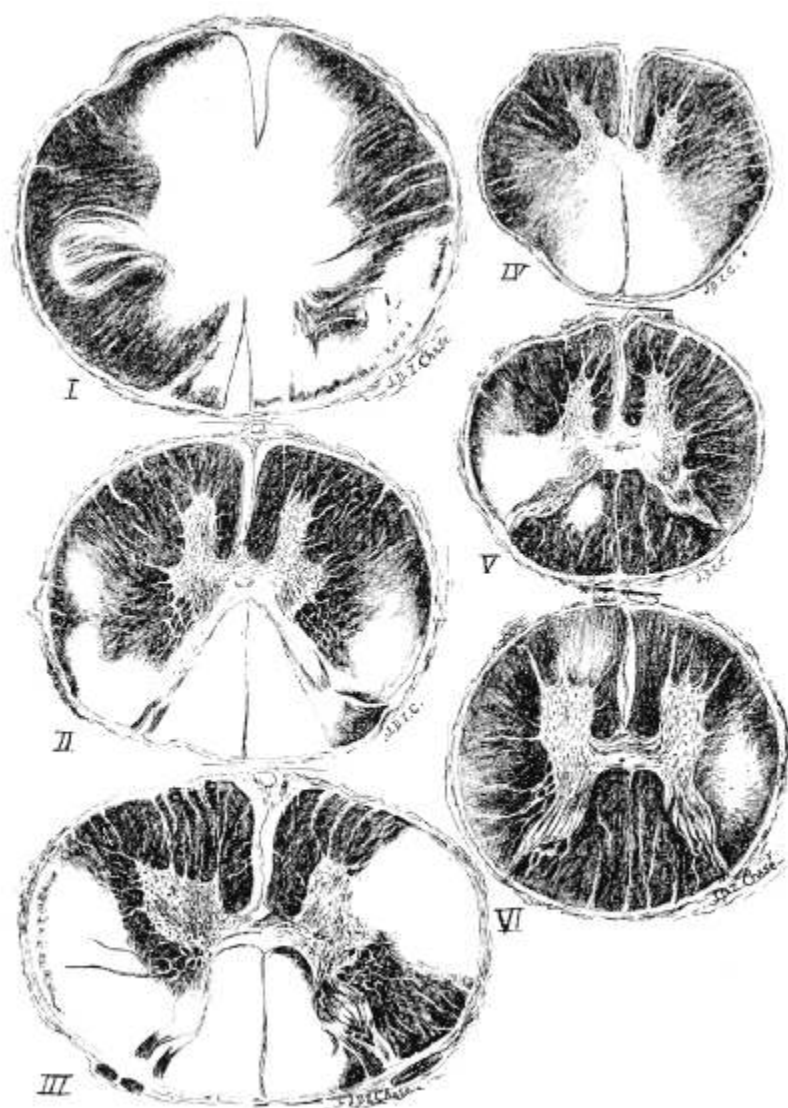
He died suddenly a few weeks after our examination.

Necropsy revealed the following: The central nervous system—On gross examination isolated areas of sclerosis scattered irregularly over the bulb and cord were visible. These patches varied in color, some being yellow, others gray, and still others of a gelatinous appearance, at times so indistinct as to be overlooked and detected only in the stained specimen. These latter areas were sometimes very extensive. The microscopic

examination of the cord revealed extensive degeneration following in places the type of system degeneration, *i. e.*, confined to the lateral or postero-lateral tracts; at other places affecting the cord irregularly. In the dorsal cord the areas were very numerous and irregular in distribution. (See Figs. iv and v.) Only the ninth and eleventh segments were free, the others having one or more areas of sclerosis. The lumbar enlargement was comparatively free, there being only one small patch of sclerosis in the third lumbar. The medulla oblongata contained several areas of degeneration: one of these extended from the ventral to the dorsal surface; the other areas were irregularly unilateral. The twelfth nucleus was involved, but the cells showed no other change than excessive pigmentation. The pontine lesions consisted of several areas mostly limited to the right side of the pons, although several minute areas were present on the left side. On the right a rather extensive patch extended along the ventricular surface embracing the sixth and seventh nuclei, and involving the inferior surface of the cerebellum. The basal ganglia were free. Several small patches were scattered through the centrum semi-ovale, and very extensive areas were present in the neighborhood of the inferior horn of the lateral ventricle.

The cerebral cortex presents many interesting features. On gross examination of the Müller hardened specimen, extensive areas stained a light yellow without differentiation from the underlying white matter. Under the microscope these degenerated areas contained no tangential fibers. The white substance for several millimeters remained unstained and contained many compound granule cells filled with a pigment staining black with the Weigert method. The glia cells were also markedly enlarged and contained the same pigment. The ganglion cells were very scarce and were very yellow from pigment and rarely shrunken and atrophied. The vessel walls showed evidence of irritation, in some places being thickened, in others surrounded by a reticular network of nucleated cells. The optic nerves and commissure were almost completely destroyed by extensive areas of sclerosis. The right optic nerve contained practically no myelin at all. Two-thirds of the left nerve was likewise affected. The commissure on cross section contained a small crescent of stained fibers around either end of the section. The other cranial nerves were not affected.

We have, in short, a case which, during a course of seven years, presents the clinical picture of a posterior sclerosis; of an ataxic paraplegia (postero-lateral sclerosis); and imme-



The drawings represent the areas of sclerosis in different portions of the spinal cord.

diately before death of a spastic paraplegia; the typical symptoms of multiple sclerosis never at any time being present.

That a disease process so extensive and irregular in its involvement of nervous tissue, so irregular in its etiology and development, should fail to follow any one clinical type is rather to be expected than otherwise. It is not surprising, therefore, that several irregular or atypical forms should be found described. Besides the usual cerebro-spinal form we have the cerebral and the spinal form, the bulbar, the myopathic and optic varieties. We have a still further division into the acute, subacute, and chronic, according to the course of the disease. These different forms run one into the other, but besides the different cases which may be arranged under these various headings there are many which cannot be so classified and are described as atypical forms. The diagnosis in our case was made difficult not only by the entire absence of what are usually considered the typical symptoms of multiple sclerosis, *i. e.*, the intention tremor, scanning speech, nystagmus, loss of mental power, etc.; but also by the course of the disease itself, which, by picking out certain system tracts of the cord at successive intervals, led to the diagnosis by different observers of the disease suggested by the tracts affected. The diagnosis of *tabes dorsalis* made at the onset is easily explained by the pathological examination. A dense and by far the oldest plaque of sclerosis is found in the dorsal region and is almost entirely limited to the posterior columns. (See Fig. iv.) In no other area affected is there such complete destruction of both myelin sheaths and axis cylinders, and in no other area does the glia take on such a wavy and fibrillar appearance on long section as here. A differential diagnosis in this stage would certainly be very difficult. Whether the eye-grounds at this period presented any changes it is impossible to state, but inasmuch as the patient did not complain of even haziness of vision for a year or so later it is probable that no change existed. Granting such to be the case, the absence of pain becomes an important negative symptom, and a possible determining factor between lesions affecting the posterior columns and those in which the roots are also in-

volved. With involvement of the lateral tracts spasticity was added to the other symptoms, and under a different observer ataxic paraplegia (combined system disease) was diagnosed. The lesions in the cervical cord show a much more advanced degree of sclerosis than the dorsal or cerebral lesions, and it was probably these lesions which caused the symptoms. (See Figs. ii and iii.) The lateral and posterior columns are much more likely to be affected in cervical sclerosis than other portions of the cord. We find this to a certain extent true in the cases of others where we have been able to examine the diagrams of the affected cords. The differential diagnosis at this stage would still be very difficult, but might have been suggested by the partial optic atrophy which probably developed at this time. When the case came under our observation the loss of power was so extensive and the spasticity so great that it was impossible to determine any ataxia even had it been present. Unaware of the previous diagnoses, and in the absence of sensory or other localizing symptoms, a provisional symptomatic diagnosis of spastic paraplegia was made. The eye examination would, in all probability, have made a correct diagnosis possible, but was not made on account of lack of proper facilities and because the patient did not complain of any failing vision, and even the night before his death wrote some letters.

The case presents many interesting and instructing features. It suggests the importance of a careful eye-ground examination in that large class of cases too frequently diagnosed spastic paraplegia, meaning, of course, primary degeneration of the motor tracts, and which almost invariably turn out post-mortem to be something else. Attention has already been called to the frequency of ocular symptoms in multiple sclerosis. The changes to be expected are complete or more frequently partial optic atrophy, pallor and loss of definition of the temporal side of the disc, hyperemia of the disc, and rarely optic neuritis. These changes may be the initial symptoms and lead to early diagnosis. Of fifty cases analyzed by Grauck, fifteen revealed changes in the fundus, nineteen with pupillary changes, four of which showed rigidity of the pupil.

Such changes, even when very extensive, may be accompanied, as in our case, with comparatively little disturbance of vision.

That the complete absence of bulbar symptoms (scanning speech, wasting of the tongue, etc.) does not necessarily imply the freedom of the bulb from sclerotic patches is fully proven by the extensive involvement of both pons and medulla in this case. The contention of Erb and Ordenstein that lesions of the pons are the cause of the intention tremor would seem to be disproven by the findings in our case. If such were the case we would expect this symptom in a marked degree on one side on account of the very extensive involvement of the right half of the pons and the almost complete exemption of the left. The widespread involvement of the cerebral cortex by a degenerative process, on the right side spreading over the entire motor area and parietal lobe, and on the left over the temporo-sphenoidal and occipital areas would likewise contravert Greif's assumption that this area (motor) was at fault. The thalamus was entirely normal, and in so far supports the theory of Stephan that thalamic lesions are the cause of intention tremors in this disease. The occurrence of intention tremor in fifty per cent. of the cases, and the comparative frequency of the involvement of the basal ganglia also support this view. The presence of nystagmus in a large per cent. of all cases is interesting in connection with its absence here. The cerebellum, to which this symptom has been attributed, was only slightly involved by a patch of sclerosis extending from the ventricular surface of the pons.

The absence of sensory symptoms was probably accidental; sensation being intact on those occasions when a careful examination for sensation was made. There must necessarily have been sensory changes during the more acute stages of such lesions, *i. e.*, the one in the dorsal region which practically cut off the entire cord, there being only a semi-circle of unaffected tissue around the anterior median fissure. Oppenheim has called attention to the fact that unless the patient has been under observation for a long time and repeated and careful tests made, the sensory phenomena are likely to be overlooked. The sclerotic areas in the cord followed in a

general way two types: Some beginning at the margin and extending inwards, and others beginning near the central canal or at the junction of the gray and white matter (*Grenzschicht*) and extending outwards. In some of the areas of earlier formation the perivascular tissues have a peculiar structure. In those portions of the cord which approach the normal, there being no part where some proliferative change has not taken place, the vessel walls show little if any change. In areas a little further advanced, where the sclerosis is extensive enough to show grossly by the Weigert method, the vessels are surrounded by a reticular tissue which, on closer examination is seen to consist of transparent cells with distinct nuclei. In the early stage of this formation these cells are separated from the surrounding tissue by a distinct wall of cellular tissue. In other portions of the same section this reticular formation extends irregularly into the surrounding white substance. We are led to believe, on account of its structure, its close and constant association with the vessels, its presence in connection with slight thickening of the vessel walls in the early sclerosis, and its absence with marked thickening of the vessel walls in areas of advanced sclerosis, that it is the result of irritation of the vessels by the processes at work in the production of the sclerotic areas. It is also probable that these cells, connective tissue in nature, are productive factors in association with the proliferating glia in the formation of the sclerotic patches. This reticulum has nothing in common with that described by Redlich and others, due to a falling out of the axis cylinder without a concomitant overgrowth of glia. The retention of the axis cylinder in areas of dense sclerosis after complete destruction of the myelin, so commonly seen in this disease, was present to a considerable degree. We think, however, that in certain areas they were too few in number (less than in many cases of tabes) to explain the absence of secondary degeneration by their presence. We have no other explanation for these phenomena.

Such widespread cortical changes we have never seen in multiple sclerosis. On macroscopic examination the Weigert section gave us the impression of a layer of white matter

1-16 of an inch thick, in the position where the tangential fibers lie. This proved to be a layer of Deiters' cells several deep, filled with pigment staining black with hematoxylin. Beneath this an unstained area at least twice as broad as the cortical gray substance indicated the depth to which the process had extended. The presence in those areas of the nerve cells practically intact is what we might have expected from sclerosis of the gray substance of the cord in this and other cases, and explains the lack of mental symptoms, although his inactive life gave little opportunity for judging of the mental acuity which was necessary in his occupation.

- 139 HERZEN KRANKHEIT UND EPILEPSIE (Relation of Heart Disease to Epilepsy). R. Stintzig (Deutsch. Archiv f. klin. Med., Vol. 66, Dec. 13, 1899, p. 241).

Stintzig reports 2 cases of this condition occurring respectively in a girl of 23 and in a young man of 32; in the former both conditions developed apparently as the result of a severe injury to the breast at the age of 18. From this time there was dyspnea and palpitation of the heart. The treatment of the heart condition seemed to have little effect upon the frequency of the convulsions, nor did they on the other hand produce any alteration apparently in the compensation of the heart. At her death the brain was normal; there was tricupsid mitral obstruction. The second patient developed epilepsy at the age of 22 and the heart disease apparently some time later. He was a chronic alcoholic, and finally died in *status epilepticus* produced by a prolonged debauch. There was mitral obstruction. Stintzig believes that there are three possibilities: either the epilepsy and the heart disease develop as a result of a common cause or they are accidental complications; or one disease may produce or influence the course of the other. He believes that in certain cases some common cause, such as syphilis, may actually produce both conditions. He is skeptical, however, as to whether epilepsy could ever produce heart disease, and thinks it possible that heart disease could only produce epilepsy in a person strongly predisposed to it. The majority of cases in which the complication occurs are youthful individuals. He concludes that the simultaneous occurrence of epilepsy and heart disease is usually accidental; that epilepsy may produce transitory dilatation; that heart disease cannot be the only cause of epilepsy; but may, under certain circumstances perhaps by producing disturbances in the circulation of the brain, contribute to the cause of the epileptic attacks. In some conditions, treatment of the cardiac condition assists the epilepsy; in others the epileptic attacks may be replaced or accompanied by angina pectoris. SAILER.